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EXAMINER	
JAGOE, DONNA A	
ART UNIT	PAPER NUMBER
1619	
MAIL DATE	DELIVERY MODE
03/18/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,000	ARBER ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/4/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-45 are presented for examination.

Preliminary Amendments

The preliminary amendment the specification filed April 16, 2009 has been entered.

The preliminary amendment to the claims filed August 10, 2006 has been entered.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 35-41 are is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claims 35-41 are rejected under 35 U.S.C. 101 because the claimed invention is directed to both a "process" of use and a process of making. The claim embraces or overlaps two different statutory classes of invention set forth in 35 U.S.C. 101 which is

drafted so as to set forth the statutory classes of invention in the alternative only. *Ex parte Lyell*, 17 USPQ2d 1548 (Bd. Pat. App. & Inter. 1990) *Id.* at 1551.

One interpretation of instant claims 35-41 is "method of use" claims. In order to advance prosecution in this case, 35-41 will be interpreted as "**method of use**" claims.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-4, 10, 11, 25, 34-41 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 35-41 provides for the use of curcumin and a NSAID for the preparation of a formulation, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

The term "susceptible" in claim 34 is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a reasonable standard for ascertaining the requisite degree, and thus one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Since no guidance is provided as to how immune a given value can be and still fall within the scope of the instantly claimed subject matter as circumscribed by the term "susceptible"

the metes and bounds of the term are not clear, making it impossible to ascertain with reasonable precision when that term is infringed and when it is not.

Claims 2-4, 10, 11 are rejected as being indefinite because a medicinal chemistry definition of analog is: An analog is a drug whose structure is related to that of another drug but whose chemical and biological properties may be quite different. The Examiner is unclear on the structure and or possible functions of an analog of curcumin. The specification does not make it clear exactly what an analog might be other than demethoxycurcumin and bisdemethoxycurcumin identified as an “analog or derivative” in instant claim 5.

Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. The claim is drawn to the composition comprising one or more additional active ingredients, selected from agents suitable for combination therapy. There is no guidance in the instant specification to direct one to any specific agent other than what is recited specifically in the claim thus rendering the claim indefinite because the claim includes elements not actually disclosed (those encompassed by "and other agents suitable for combination therapy"), thereby rendering the scope of the claim unascertainable. See MPEP § 2173.05(d).

Claim 43 recites the limitation "a dosage unit of the vaccine" in line 2 of the claim. There is insufficient antecedent basis for this limitation in the claim because there is no recitation of a vaccine in claim 33 from which it depends.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7, 16, 19-21, 25-28, 30, 32 and 34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibiting cancer cell growth in a subject it does not reasonably provide enablement for preventing or treating cancer or reducing the likelihood of contracting cancer in a subject susceptible to contracting said disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

A. Breath of the Claims: The complex of nature of the claim is greatly exacerbated by breath of the claim. The claims encompass prevention and reducing the likelihood of contracting of cancer in an individual which have

potentially many different causes (Current evidence indicates that cancers are caused by abnormalities in the genetic material of the transformed cells. These abnormalities may be due to the effects of carcinogens, such as tobacco smoke, radiation, chemicals, or infectious agents. Other cancer-promoting genetic abnormalities may randomly occur through errors in DNA replication, or are inherited, and thus present in all cells from birth. The heritability of cancers is usually affected by complex interactions between carcinogens and the host's genome. Also, cancer affects people at all ages with the risk for most types increasing with age). Each of these defects may or may not be addressed by the administration of the claimed compounds.

B. Nature of the Invention: Claims 7, 16, 19-21, 25-28, 30, 32 and 34 are drawn to a for use in the prevention or treatment of cancer or reducing the likelihood of contracting cancer in a subject susceptible to contracting said disease. The nature of the invention is extremely complex in that it encompasses the actual prevention of a cancer such that the subject treated with above compounds does not contract cancer. As explained supra, there are many causes for cancer making the prevention this disease unpredictable. Further, the instant specification defines “treatment of cancer” as “prevention for prophylactic situations for those patients susceptible to contracting cancer” (page 15, lines 9-18). As stated supra, the instant claims recited do not reasonably provide enablement for preventing or treating cancer or reducing the likelihood of contracting cancer.

C. State of the Prior Art: While the state of the art is relatively high with regard to inhibiting cancer cell growth, the state of the art with regard to **prevention** of such disorders is underdeveloped. In particular, there do not appear to be any examples or teachings in the prior art wherein cancer was predictably prevented because cancer is a diverse class of diseases which differ widely in their causes and biology.

D. The Level of One of Ordinary Skill: The relative skill of those in the art is generally that of a physician.

E. Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual prevention of cancer or reducing the likelihood of contracting cancer in a subject susceptible to contracting said disease makes practicing the claimed invention unpredictable in terms of **prevention** or treatment or prophylaxis of cancer, even in a subject that is susceptible to the disease.

F. Guidance of the Specification: The guidance given by the specification as to how one would administer the claimed compounds to a subject in order to actually prevent cancer is minimal. All of the guidance is drawn to prophylactic situations wherein it is unclear whether one would have contracted cancer without the administration of the composition of curcumin and a NSAID.

G. Working Examples: All of the working examples provided by the specification are drawn to in vitro effects on cancer cell lines.

H. The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for **prevention or treatment** of cancer or reducing the likelihood of contracting cancer. If unsuccessful, which is likely, given the lack of significant guidance from the specification or prior art with regard to the predictable prevention of cancer with any compound, one of skill in the art would have to then either envision a modification of the curcumin and NSAID, dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance from the specification of prior art regarding prevention of cancer, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to prevent the development of cancer or reduce the likelihood of developing cancer in a susceptible subject by administration of a combination of the NSAID and curcumin.

Therefore, a method of prevention or treatment and reducing the likelihood of contracting of cancer in an individual by administering an NSAID and curcumin is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5-24, 26-41 are rejected under 35 U.S.C. 102(b) as being anticipated by Metaproteomics LLC WO 03/007975 A1.

Metaproteomics teach synergistic compositions comprising curcuminoids and non steroidal anti-inflammatory agents (NSAIDs) such as diterpene lactone species and triterpene species, known for their anti-inflammatory properties, (page 3, lines 18-25) for the treatment of inflammatory diseases such as arthritis (page 1, lines 30-34) and treatment of cancer such as colorectal cancer (page 2, lines 1-3). It further teaches that the compounds can be administered together such that they are synergistic so that they can be used at sufficiently low doses with no adverse side effects and wherein the COX-2 specificity is < 5-fold (page 3, lines 26-33). Demethoxycurcumin and bisdemethoxycurcumin are disclosed as curcumins that are included in the invention (page 8, lines 15-17) (claim 5). Regarding claims drawn to administration of the agents separately or together, Table 9 teaches administration of first compound (curcumin), second compound (oleanolic acid) and the two components combined (table 9, page 22). Addressing claim 14 drawn to contacting cells with a formulation containing curcumin and at least one NSAID, Example 8 (page 25) teaches treatment of colon

cancer comprising administration of the composition. Addressing instant claims 22 and 33, drawn to the pharmaceutical composition comprising curcumin and at least one NSAID and a pharmaceutically acceptable carrier, excipient or diluent, Metaproteomics LLC teach the compositions formulated in a pharmaceutically acceptable carrier (page 26, lines 25-29).

Claims 18- 25, 33 and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Gelber et al. Patent Application Publication US 2001/0044410 A1.

Gelber et al. teach a composition comprising a **NSAID** (see claim 3) and an anti-inflammatory nutriceutical such as **curcumin** (see claim 9) and further comprising **carriers** (paragraph 68) and other agents that are suitable for combination therapy, such as Goldenseal (paragraph 30) which is an immune booster with **antibiotic** activity.

Claim 29 is rejected under 35 U.S.C. 102(b) as being anticipated by O'Neill et al. U.S. Patent No. 4,704,405.

The claim is drawn to a composition comprising a NSAID for treatment of inflammation. O'Neill teaches a composition comprising an NSAID (column 1, lines 13-15) for treatment of inflammation (column 2, lines 34-35).

Claims 30 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Arbiser U.S. Patent No. 6,673,843 B2 (reference AC from IDS dated 1/4/07).

The claims are drawn to a pharmaceutical composition comprising curcumin for treatment of cancer and inflammation. Arbiser teaches administration of curcumin for treatment of inflammation (column 5, lines 37-57) and cancer (see abstract).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Metaproteomics LLC WO 03/007975 A1. as applied to claims 1, 5-24, 26-41 above, and further in view of Reddy et al. (reference AS from IDS dated 1/4/07).

Metaproteomics teach synergistic compositions comprising curcuminoids and non steroidal anti-inflammatory agents (NSAIDs) such as diterpene lactone species and triterpene species, known for their anti-inflammatory properties, (page 3, lines 18-25) for the treatment of inflammatory diseases such as arthritis (page 1, lines 30-34) and treatment of cancer such as colorectal cancer (page 2, lines 1-3). It further teaches that the compounds can be administered together such that they are synergistic so that they can be used as sufficiently low doses with no adverse side effects and wherein the COX-2 specificity is < 5-fold (page 3, lines 26-33). It does not teach the NSAIDS selected from, for example sulindac. However, Reddy et al. teach that sulindac is a NSAID (page 157, column 2). It is prima facie obvious to substitute equivalents, motivated by the reasonable expectation that the respective species will behave in a comparable manner or give comparable results in comparable circumstances. The express suggestion to substitute one NSAID for another need not be present to render the substitution obvious. It would have been obvious to substitute the anti-inflammatory agents such as ursolic acid of Metaproteomics LLC for the NSAID sulindac of Reddy et al. The prior art showed that ursolic acid has inflammatory effects and works synergistically with curcumin to treat inflammation and cancer, therefore, it would have been obvious to one of ordinary skill in the art to substitute the sulindac taught in Reddy

et al. for the ursolic acid of Metaproteomics LLC for the predictable result of treatment of cancer and inflammation.

Claims 42-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Metaproteomics LLC WO 03/007975 A1.

Addressing instant claims 42-45, drawn to a kit, it is a standard of practice in the pharmaceutical arts to enclose a composition in a vessel, and to enclose instructions for use in a package. Given that the curcumin and NSAID composition of Metaproteomics LLC is for use by a human to treat inflammation and cancer, it would have been *prima facie* obvious to one of ordinary skill in the art to include instructions as to how to administer the contents of the article for that purpose. Because the printed matter in the instructions has no functional relation with the substrate on which it appears, it does not distinguish the claimed invention over that of Metaproteomics. *See In re Gulack*, 703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983). Hence, the kit recited in instant claims 42-45 would have been *prima facie* obvious to one of ordinary skill in the art over the Metaproteomics LLC reference.

Thus the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Accordingly, for the above reasons, the claims are deemed properly rejected and none are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne (Bonnie) Eyler can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/YVONNE L. EYLER/
Supervisory Patent Examiner, Art Unit 1619

Donna Jagoe /D. J./
Examiner
Art Unit 1619

March 10, 2010